Docket No. 20784/4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Demuth, et al. EXAMINER:

SERIAL NO.: 09/___,___ ART UNIT:

FILED: December __, 2000 (HEREWITH)

FOR: PRODRUGS OF DP IV INHIBITORS

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CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as EXPRESS MAIL in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on: December 21, 2000.

By: Renee M. Mason-Salewala

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COMMISSIONER OF PATENTS AND TRADEMARKS
WASHINGTON, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to examining the above-entitled patent application and before calculating the filing fees, please make the following amendments:

In The Specification:

On the 1st page following the title and before Field of The Invention, please insert the following:

--The present application is claiming priority of DE 198/28113.7 filed on June 24, 1998 and subsequent PCT EP 99/04382 application filed on June 24, 1999.

In the Claims:

1. (AMENDED) Prodrug compounds of inhibitors of the enzymatic activity of dipeptidyl peptidase IV (DP IV), which [prodrug]compounds have the general formula A-B-C, wherein
A is an amino acid,
B is a chemical bond between A and C or is an amino acid, and
C is a stable inhibitor of DP IV without C-terminal phosphonate residue.

2. (AMENDED) [Prodrug]The compounds according to claim 1, wherein [characterised in that] B is selected from a group consisting of proline, hydroxyproline, thiazolidinecarboxylic acid, dehydroproline, pipecolic acid, azetidinecarboxylic acid or aziridinecarboxylic acid.

3. (AMENDED) [Prodrug]The compounds according to claim 1 [or 2, characterised in that] wherein[,] B is selected from a group consisting of proline or hydroxyproline.

4. (AMENDED) [Prodrug]The compounds according to claim 1 wherein said stable inhibitor [one of the preceding claims, characterised in that C] is selected from a group consisting of [an] aminoacylpyrrolidide, aminoacylthiazolidide or N-dipeptidyl, O-acyl hydroxylamine.

5. (AMENDED) [Prodrug]The compounds according to claim 1 [one of the preceding claims, characterised in that the] wherein said stable inhibitors are present in salt form.

6. (AMENDED) [Prodrug]The compounds according to claim 1 [one of the preceding claims, characterised in that] wherein A-B is a dipeptide of formula Ile-Pro or Gly-Pro.

7. (AMENDED) A [P]pharmaceutical composition [, especially] for oral administration containing prodrug compounds of inhibitors of dipeptidyl peptidase IV wherein [characterised in that it comprises] said composition comprises at least one prodrug compound [according to one of the preceding claims] optionally in combination with customary carriers or excipients.

8. (AMENDED) A method of using [Use of prodrug] compounds of stable inhibitors of dipeptidyl peptidase IV [or] in a pharmaceutical compositions [according to one of the preceding

claims] in the preparation of a [medicament] pharmaceutical composition for the temporally controlled *in vivo* inhibition of DP IV comprising providing a compound of the general formula A-B-C, wherein

A is an amino acid,

B is a chemical bond between A and C or is an amino acid, and

C is a stable inhibitor of DP IV without C-terminal phosphonate residue.

9. (AMENDED) The method of claim 8 [Use of prodrug compounds or pharmaceutical compositions according to one of claims 1 to 6] wherein said use is in cell[-], tissue[-] or organ[-]specific enzymatic inhibition of DP IV.

10. (AMENDED) A method of treating [Use of prodrug compounds or pharmaceutical compositions according to one of claims 1 to 6 in the treatment of] metabolic disorders in mammals that can be treated by modulating the DP IV enzymatic activity of a mammal comprising of the step of administering to said mammal a compound of the general formula.

11. (AMENDED) The method of claim 10 [Use according to claim 9] wherein said treatment is in the treatment of metabolic disorders in humans.

12. (AMENDED) The method of claim 10 [Use according to claim 9] wherein, said compounds are used to treat[in the treatment of] impaired glucose tolerance, glucosuria, hyperlipidaemia, metabolic acidoses, diabetes mellitus, diabetic neuropathy, obesity and nephropathy and of sequelae of diabetes mellitus in mammals.

13. (NEWLY ADDED) The compounds of claim 1 wherein said compounds comprise said stable inhibitor of DP IV within a complex comprising said prodrug, said prodrug preventing the degradation and increasing the activity of said stable inhibitors.

REMARKS

No new matter has been added as a result of the above-presented amendments.

The Applicants respectfully request expeditious consideration and allowance of the present application. The Examiner is invited and encouraged to telephone the undersigned if such would serve the furtherance of the prosecution of the present application.

Respectfully submitted,

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